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Gerald Adams

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HOFFMANN & BARON, LLP
6900 JERICHO TURNPIKE
SYOSSET, NY 11791

EXAMINER

CRAIGO, WILLIAM A

ART UNIT

PAPER NUMBER

1615

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/591,369	Applicant(s) ADAMS ET AL.	
	Examiner WILLIAM CRAIGO	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 March 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 17-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 and 26-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 September 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Acknowledgement is made of the response filed 19th March, 2010. In that response claims 1, 2, 3, 4, 5, 8, and 14 were amended. Claims 27-30 were added.

Withdrawn Rejections

Rejections not expressly maintained in this action are withdrawn.

New Rejections Necessitated by Amendment

Claim Objections

Claims 8 and 9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 8 recites the identical component "additive/stabilizer" in the same range "0.1 to 10% by weight" as recited in instant claim 1. Claim 9 is objected to because it depends from claim 8.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

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was filed, had possession of the claimed invention. In the instant case, claim 1 has been changed in scope by the transitional phrase "consisting of". There are no examples in the specification nor is it clearly communicated in the specification that the scope be limited in the manner claimed. There are no examples containing "from 0.1 to 10% by wt of additive/stabilizer" as claimed. For example the specification at [0046] states the additive/stabilizer is optional and there are no examples containing an additive/stabilizer as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 and 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 states the excipient is crystalline, and then states "wherein where the excipient is amorphous". If the excipient is crystalline, it cannot also be amorphous. The metes and bounds for which applicant is claiming protection is unclear.

Claims 3, 4, 5, 9, and 27-30 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, the claims recite the transitional phrase "comprising", this is indefinite because they depend from claim 1 which recites the transitional phrase "consisting of". The metes and bounds for which applicant is claiming protection are unclear because the dependent claims appear to be broader in scope than the independent claim from which they depend.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 26 is rejected under 35 U.S.C. 102(b) as being anticipated by Maa, WO02/101412 A2.

Maa, pg. 60, table 2.9, batch 156-35-1 discloses a powdered formulation comprising 10 % BSA (sensitive active material) and 90 % excipients. At least the excipient trehalose is amorphous meeting the limitation of "at least 0.1% of the mixture is in an amorphous state".

Maa anticipates the subject matter of instant claim 26.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-16 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maa, WO02/101412 A2 in view of Chen, J. Pharm. Biomed. Anal., 26, 2001.

Maa is directed to freeze dried compositions of a powder form comprising a pharmaceutical agent (i.e. sensitive active material).

Maa, pg. 26, lines 4-7, teaches excipients including dextrose, sucrose, lactose, trehalose, mannitol, sorbitol, inositol, dextran, starch, cellulose, sodium or calcium phosphates, calcium carbonate, calcium sulfate, sodium citrate, citric acid, tartaric acid, glycine, high molecular weight polyethylene glycols (PEG), and combinations thereof.

Maa, pg. 26, lines 17-27 teaches crystalline and amorphous excipients for use in stabilizing the active material. Maa, pg 27, lines 8-12 and claim 7 teaches amorphous lactose (compare instant claim 1), monosaccharides, disaccharides, oligosaccharides

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and polysaccharides (compare instant claim 6); lines 13-14 teach crystalline mannitol and sorbitol (compare instant claims 1 and 7).

Maa, pg. 28, line 8-9 teaches the addition of a surfactant (1-5 wt%) for stabilizing the active material, and formulation 156-16-1 (pg. 57) teaches a surfactant at 0.1wt% (compare 0.1 to 10% by wt of additive stabilizer, claim 1). Maa, pg. 57, formulation 156-16-2 teaches 0.1% methionine (antioxidant, compare instant claims 8-9). Maa teaches the excipients are chosen to maintain low hygroscopicity of the powders (Maa, pg. 26 line 19), providing a showing that reducing the hygroscopicity of powdered formulations was a known problem in the art at the time the invention was made (compare instant claims 13 and 14).

Maa, pg. 20, line 23 teaches polypeptide, compare instant claim 10. Maa, pg. 22, line 14 teaches bacterium, compare instant claim 11. Maa, pg. 27, line 14 teaches the composition is comprised of a crystalline excipient with an amorphous excipient, compare instant claim 12. Maa, pg. 34, line 17, teaches a single unit dosage, compare instant claim 15. Maa, pg. 34, line 20 teaches a sterile formulation package, compare instant claim 16.

Maa, pg. 28, lines 3-4 teaches amorphous excipients present in an amount from 10 to 90 wt%; and a crystalline excipient in an amount from 10 to 90 % by weight. This teaching suggests to the skilled artisan the ranges: from 0.01 to 50 wt% of the sensitive active material (compare instant claims 1, 3, 4, 26, 27, 28); from 0.1 to 50 wt% (instant claim 1) and 1 to 50 wt% (instant claim 2) of the mixture is in an amorphous state; 50 to 99.99 wt% of the excipient in the crystalline state (compare instant claim 3); 50 to 99.89

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wt% of the excipient in the crystalline state (compare instant claim 4); 75 to 99.49 wt% of a crystalline excipient (compare instant claim 5); from 50 to 99.99 wt% of the excipient (compare instant claim 26) from 50 to 99.9 wt% of the excipient (compare instant claim 29); and 50 to 99.5% by weight of the excipient (compare instant claim 30).

In the case where the claimed ranges “overlap or lie inside ranges disclosed by the prior art” a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). **MPEP 2144.05**

While Maa teaches a lower limit of 10 wt% for amorphous excipients and that the excipients should be chosen to minimize the hygroscopicity of the formulation, Maa does not expressly teach amorphous excipients below 10 %; however there was motivation in the art to minimize the amount of amorphous components in a formulation.

Chen is directed to determining the amount of amorphous content of lactose in pharmaceutical formulations. Chen, introduction, pg. 1, teaches lyophilization can induce amorphous forms of components in formulations. Chen, pg. 2 teaches that amorphous fractions result in higher hygroscopicity and lower chemical stability than the crystalline phase. Chen provides express suggestion to the skilled artisan to reduce the amorphous fraction of components in pharmaceutical formulations.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the prior art elements of Maa and Chen according to known methods to yield the predictable result of providing a stable powdered formulation as instantly claimed because Maa teaches stable formulations

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and Chen expressly teaches reducing the amorphous fraction in formulations provides improved stability and reduced hygroscopicity to pharmaceutical formulations.

Maa provides a showing that powdered formulations with the substantially the same excipients and sensitive active materials were known in the art. Chen provides a showing that reducing the amorphous content of lyophilized (i.e. powdered) formulations was expressly known in the art. One of ordinary skill could have combined the teachings of both references using routine experimentation with a reasonable expectation of success and the combination yields no more than predictable results to one of ordinary skill in the art.

Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). **MPEP 2144.05**

As the combined teachings of Maa and Chen teach substantially the same elements in substantially the same arrangement as instant claim 1, the formulation necessarily has the properties recited in instant claims 13-14. See MPEP 2112.01.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).

“When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the

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prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

The combination of Maa and Chen recite components which meet the structural limitations, and which appear to be in the same arrangement as recited in instant claim 1; since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is shifted to Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), see MPEP 2112.

As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972), see MPEP 2113.

Accordingly, the subject matter of instant claims 1-16 and 26-30 would have been prima facie obvious to one of ordinary skill at the time the invention was made, particularly in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to WILLIAM CRAIGO whose telephone number is

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(571)270-1347. The examiner can normally be reached on Monday - Friday, 7:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/WILLIAM CRAIGO/
Examiner, Art Unit 1615

/Leon B Lankford/
Primary Examiner, Art Unit 1651